THE INFLUENCE OF SODIUM AMYTAL ON URINARY EXCRETION*

By LUDWIG A. EMGE, M. D.
AND
P. E. HOFFMANN, M. D.
San Francisco

IN the introduction of any drug which is likely to find universal usage we must, above all, be certain that its margin of safety is such that even in the hands of the less experienced and the less cautious the effect of the drug will not create a state of serious danger to the life of the patient. Whenever dramatic and spectacular reactions overshadow dangers not easily discerned we must then make doubly sure to discover all possible sources of danger. This applies particularly to the barbituric acid derivatives which, when given in sufficiently large doses to induce deep hypnosis, are known to produce vasomotor and respiratory depressions of major importance easily overshadowed by the dramatic action of these drugs. The only difference between the various barbituric acid derivatives which are otherwise quite similar in their therapeutic and pharmacologic action is their respective toxicity determined by their margin of safety as expressed in minimal lethal doses found experimentally in animals. Since man may be more susceptible to the action of barbiturates than most animals any dosage which approaches 50 per cent of the minimal lethal dose for animals used to induce degrees of surgical anesthesia in man therefore constitutes a potential source of danger. As far as it has been determined experimentally, barbital or veronal carries the widest safety margin which narrows itself down to about one-third when amytal (isoamylethyl barbituric acid) and neonal (cyclohexenylethyl barbituric acid) are reached.

PURPOSE OF THESE STUDIES

Because of these factors we have recently undertaken a detailed study of the immediate and more distant effects of the barbiturates on women when given in sufficient amounts to induce deep hypnosis as a preliminary to inhalation anesthesia. Through the courtesy of Eli Lilly & Company, sodium isoamylethyl barbiturate (hereafter designated as sodium amytal) has been furnished us as part of the material for this study. Since recently there has been aroused a good deal of interest in the action of this particular barbiturate, we wish to make a preliminary report on a comparative study involving fluid intakes and outputs and sulphophenolphthalein excretions in surgical and obstetrical patients.

I. ITS USE IN TWO SURGICAL GROUPS

This study covers approximately fifty patients undergoing major operations of a similar nature and severity divided into two fairly equal groups. In one group we used as a preliminary to nitrous oxid anesthesia, sodium amytal and morphin, and in the other scopolamin and morphin.

About one-half hour before operation Group A received, according to body weight, up to fifteen grains of sodium amytal by mouth on the basis of one-tenth grain per pound of body weight, or an equivalent amount by intravenous administration according to the blood-pressure reactions. In addition, one-sixth to one-fourth of a grain of morphin sulphate was given hypodermically prior to taking the patient to the operating room. Except for the ability to gauge the dose slightly more accurately by intravenous administration, we did not see any material difference in the hypnotic end reaction except that after oral administration it took from five to ten minutes longer for deep hypnosis to appear and to take longer to wear off in the postoperative period.

In Group B one three-hundredth of a grain of scopolamin hydrobromid (Roche) was given hypodermically one hour before the operation and repeated in thirty minutes. In addition, one-sixth to one-fourth of a grain of morphin sulphate was administered prior to sending the patient to the operating room. Operations were then carried out under nitrous oxid inhalation anesthesia with an occasional small amount of ether added. With few exceptions all patients of the two groups received normal salt solution by hypodermoclysis during the operation in order to secure a fluid balance. Fluid intake and output was then checked for three days and supplemented with sulphophenolphthalein readings whenever feasible.

After allowing for all possible variations created by age, and by length and severity of operation, our results were briefly as follows. Because of the limited space here, the detailed figures and curves shown in our study will appear elsewhere.[1]

OBSERVATIONS

1. Patients having received sodium amytal and morphin as a preliminary to inhalation anesthesia decidedly take in more fluid on the day of operation than patients having received scopolamin and morphin. At the same time the urinary output is actually and relatively decreased in the sodium amytal group.

2. Our figures show further that sodium amytal patients take fluid by mouth more readily on the day of and the day following the operation because of the greater freedom from nausea.

3. On the day following the operation the fluid intake in both groups reaches fairly equal levels, but the ratio of output again presents a lower average in the sodium amytal group. At the same time the output at times exceeds the intake in the scopolamin group.

4. On the second day after operation the fluid intake of the sodium amytal group rises above the scopolamin group, now also presenting an occasional greater output than intake. The ratio of output to intake in both groups now reaches similar levels.

5. Hoping to find the reason for these phenomena pointing to glomerular inactivity we investigated the sulphophenolphthalein excretion of

* From the Department of Obstetrics and Gynecology, Stanford University School of Medicine.

* Read before the Anesthesiology Section of the California Medical Association at the fifty-ninth annual session at Del Monte, April 28 to May 1, 1930.

patients of these two groups as well as in others. The "normal" for the individual patient was established before the operation. Variations were studied on the evening of the operation day and on the following day.

Allowing for all the possible factors which might influence these tests, we failed to find any striking differences between the sodium amytal and the scopolamin groups. There is a marked drop from the accepted "normal" on the day of operation in both groups, which is slightly greater in the sodium amytal group. The dissimilarity between the groups is so small that it must be disregarded, particularly so since on the day after operation the sulphophenolphthalein excretion approaches the accepted "normal" with equal promptness in both groups.

II. ITS USE IN PREGNANCY GROUP

We have studied the sulphophenolphthalein excretion in pregnant women during and following labor in twenty controls and twenty-one sodium amytal patients. The latter received from six to seven and one-half grains intravenously in the advanced first stage of labor, followed by supplementary nitrous oxid analgesia during the second stage. For obvious reasons studies of fluid intake and output were unsatisfactory and therefore discontinued. A comparison of the two groups studied here indicates that sodium amytal in the dosage given does not influence the glomerular activity of the kidney as expressed in per cent of sulphophenolphthalein excretion.

CONCLUSIONS

Sodium amytal and morphin, when given in sufficiently large doses to produce prolonged hypnosis, seems to allow a greater fluid intake by surgical patients on the day of and the day following the operation when compared to a similar group of patients having received scopolamin and morphin. On the other hand, urinary output is actually and relatively decreased in the sodium amytal group, more marked on the day of operation, but in neither case sufficiently marked to constitute a potential danger to the patient. It is interesting that in some instances output rises over intake in scopolamin patients twenty-four hours ahead of sodium amytal patients.

Sulphophenolphthalein excretions observed in a similar study are so slightly, if at all, influenced by sodium amytal that we may disregard the difference. Similarly, the results of this test during and after labor show no changes in sulphophenolphthalein excretions in patients having received from five to seven and one-half grains of sodium amytal intravenously.

We may therefore conclude that sodium isoamylethyl barbiturate when given orally or intravenously, while it apparently depresses urinary output, does not constitute a menace in the patient whose kidney function is otherwise normal.

2000 Van Ness Avenue.

REFERENCE

1. Am. J. of Surg., July 1930.

TRIBROMETHANOL AS A PREOPERATIVE NARCOTIC*

By DOROTHY A. WOOD, M. D.
San Francisco

TRIBROMETHANOL was discovered by Willstaetter and Duisberg during the reduction of bromal at the I. G. Farben-Industrie, Elberfeld, and was called by them "Avertin" or "E-107" as a trade mark. Chemically it is ethyl alcohol with three bromin atoms introduced into the formula or CBr3-CH2-OH, and should be called tribromethyl alcohol or tribromethanol.[1] The substance itself is a white crystalline powder which is soluble in water up to 3½ per cent at 37 to 40 degrees Centigrade. At a higher temperature the drug is decomposed, breaking down into hydrobromic acid and dibromacetaldehyd. This latter substance is highly injurious to the intestinal mucosa. Care must be taken in preparing the mixture that the water is not warmed over 40 degrees Centigrade. In all of the early experimental work the drug in powder form was used, and as quite a few deaths were reported, it was decided to dispense it in liquid form, thus simplifying the technique of preparation and lessening the danger of errors in weighing out the individual dosages. The so-called "Avertin-Fluid" is a solution of tribromethanol in amylene hydrate (itself a narcotic); one cubic centimeter of the "fluid" contains one gram of tribromethanol. This solution is extremely sensitive to air, light and heat, and must be kept tightly corked in dark bottles.

REPORTS ON TRIBROMETHANOL

After tribromethanol was discovered, it was subjected to tests and experimentation on animals before any use of it was made in human beings. The drug was then given out to different clinics for experimental use and was not available generally until one hundred thousand cases had been reported. The great mass of literature available on the subject is therefore largely in German. During the last year several articles have appeared in the English and Irish literature, but as yet no report on administration of the drug or a series of cases has appeared in American literature. It is because of the newness of the drug and the scarcity of reports in this country that we dare report so small a series as twenty-five cases, knowing full well that no true statistics can be tabulated therefrom, and only the general conclusion of caution drawn.

The early reports were full of enthusiasm for the drug not only as a narcotic but as an anesthetic. Subsequent reports bear more and more the note of caution. At the present time it is apparently agreed that the drug should be used as a "basal anesthetic" to obtain preoperative narcosis only, and should not be relied upon as the sole anesthetic agent. The danger of a fatal out-

* Read before the Anesthesiology Section of the California Medical Association at the fifty-ninth annual session at Del Monte, April 28 to May 1, 1930.